Claims

1. A method for preparing 2,3,5,6-Substituted 3*H*-Pyrimidin-4-ones comprising:

cyclizing an appropriate carbamide to obtain 2,3,5,6-Substituted 3*H*-Pyrimidin-4-ones.

2. The method as recited in claim 1, wherein the appropriate carbamide is an appropriate acetic acid 2-(1-alkyl-2-R^4-carbamoyl-alk-1-enylcarbamoyl)-phenyl ester.

3. The method as recited in claim 2, further comprising: acylation of an appropriate 3-amino-2-alkyl-alk-2-enoic acid R^4-amide to obtain the appropriate acetic acid 2-(1-alkyl-2-R^4-carbamoyl-alk-1-enylcarbamoyl)-phenyl ester.

4. The method as recited in claim 3, further comprising: reacting 2-alkyl-3-oxo-R^4-amide with anhydrous ammonia on catalysis by anhydrous aluminum chloride to obtain the appropriate 3-amino-2-alkyl-alk-2-enoic acid R^4-amide.

5. The method as recited in claim 4, further comprising: reacting 2-(2-alkyl-[1,3]dioxolan-2-yl)-*N*-R^4-alkanamide with *p*-toluenesulfonic acid monohydrate to obtain 2-alkyl-3-oxo-R^4-amide.

6. The method as recited in claim 5, further comprising: reacting 2-(2-alkyl-[1,3]dioxolan-2-yl)-alkanoic acid with oxalyl chloride followed by reaction with a primary amine to obtain 2-(2-alkyl-[1,3]dioxolan-2-yl)-*N*-R^4-alkanamide.

7. The method as recited in claim 6, further comprising: hydrolysis of 2-(2-alkyl-[1,3]dioxolan-2-yl)-alkanoic acid alkyl ester.

8. The method as recited in claim 7, further comprising: reacting of 2-alkyl-3-oxo-alkylic acid alkyl ester with ethylene glycol and *p*-toluenesulfonic acid monohydrate to obtain 2-(2-alkyl-[1,3]dioxolan-2-yl)-alkanoic acid alkyl ester.

9. The method as recited in claim 1, wherein the appropriate carbamide is an appropriate 3-R^3-carbamoylamino-2-alkyl-but-3-enoic acid methyl ester.

10. The method as recited in claim 9, wherein the 3-R^3-carbamoylamino-2-alkyl-but-3-enoic acid methyl ester is cyclized by reacting it with a primary amine and the Grignard reagent.

11. The method as recited in claim 9, wherein the 3-R^3-carbamoylamino-2-alkyl-but-3-enoic acid methyl ester is obtained by acylation of an appropriate 3-amino-2-alkyl-but-3-enoic acid methyl ester.

12. The method as recited in claim 11, wherein the appropriate 3-amino-2-alkyl-but-3-enoic acid methyl ester is obtained by reacting 2-alkyl-3-oxo-butyric acid methyl ester with liquid ammonia.

13. The method as recited in claim 1, wherein the appropriate carbamide is 2-alkyl-3-(2-alkoxy-benzoylamino)-but-3-enoic acid methyl ester.

14. The method as recited in claim 13, wherein the 2-alkyl-3-(2-alkoxy-benzoylamino)-but-3-enoic acid methyl ester is cyclized by reacting 2-alkyl-3-(2-alkoxy-benzoylamino)-but-3-enoic acid methyl ester with phenylmagnesium bromide and primary amine.

15. The method as recited in claim 13, wherein cyclizing the 2-alkyl-3-(2-alkoxy-benzoylamino)-but-3-enoic acid methyl ester yields 2-(2-alkoxy-phenyl)-3-R^4-5,6-dialkyl-3*H*-pyrimidin-4-ones, and

wherein the method further comprises reacting 2-(2-alkoxy-phenyl)-3-R^4-5,6-dialkyl-3*H*-pyrimidin-4-ones with sodium cyanide under microwave irradiation to yield 3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one.

16. The method as recited in claim 13, wherein the 2-alkyl-3-(2-alkoxy-benzoylamino)-but-3-enoic acid methyl ester is obtained by reacting 2-alkyl-3-oxo-butyric acid alkyl ester with liquid ammonia.

17. The method as recited in claim 1, wherein the 2,3,5,6-Substituted 3*H*-Pyrimidin-4-ones is at least one of:

2-(2-hydroxy-phenyl)-5,6-dimethyl-3-phenethyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(2-hydroxy-phenyl)-6-methyl-3-phenethyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-5-propyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-methoxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-5-methyl-3-phenethyl-6-trifluoromethyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-3-phenethyl-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one;

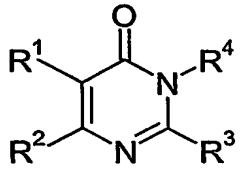
3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one;

5-cyclopropyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-3-phenethyl-3,5,6,7-tetrahydro-cyclopentapyrimidin-4-one; and

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-3,5,6,7-tetrahydro-cyclopentapyrimidin-4-one.

18. The method for preparing a compound having the chemical formula:



wherein:

R^1 and R^2 are either independently one of: H, halogen, CN, CF_3, lower alkyl, cycloalk, aryl; or R^1 and R^2 are together $-(CH_2)_n-$ and n is 5, 4, or 3;

R^3 is aryl group, which may have 1 to 4 substituents in the aryl ring each selected from the group consisting of: H, halogen, CN, CF_3, OCF_3, lower alkyl, N(lower alkyl)$_2$, lower alkoxy, OH, OC(O)-lower alkyl, OC(O)-lower alkylamino, and OC(O)-lower alkyl-N(lower alkyl)$_2$;

R^4 is H, lower alkyl, or a group of the formula $-(CH_2)_n-R^5$ wherein n is 0, 1, or 2, and

R^5 is an aryl group which may have 1 to 3 substituents on the aryl ring each selected from the group consisting of: H, halogen, CN, CF_3, OCF_3, lower alkyl, lower alkoxy, NH-lower alkyl, NH-alkylaryl, N(lower alkyl)$_2$, OH, OC(O)-lower alk, OC(O)-lower alkylamino, and OC(O)-lower alkyl-N(lower alk)$_2$;

and pharmaceutically acceptable salts or complexes;

comprising: cyclizing an appropriate carbamide to yield the compound.

19. The method as recited in claim 18, wherein the appropriate carbamide is an appropriate acetic acid 2-(1-alkyl-2-R^4-carbamoyl-alk-1-enylcarbamoyl)-phenyl ester.

20. The method as recited in claim 19, further comprising: acylation of an appropriate 3-amino-2-alkyl-alk-2-enoic acid R^4-amide to obtain the appropriate acetic acid 2-(1-alkyl-2-R^4-carbamoyl-alk-1-enylcarbamoyl)-phenyl ester.

21. The method as recited in claim 20, further comprising: reacting 2-alkyl-3-oxo-R^4-amide with anhydrous ammonia on catalysis by anhydrous aluminum chloride to obtain the appropriate 3-amino-2-alkyl-alk-2-enoic acid R^4-amide.

22. The method as recited in claim 21, further comprising: reacting 2-(2-alkyl-[1,3]dioxolan-2-yl)-*N*-R^4-alkanamide with *p*-toluenesulfonic acid monohydrate to obtain 2-alkyl-3-oxo-R^4-amide.

23. The method as recited in claim 22, further comprising: reacting 2-(2-alkyl-[1,3]dioxolan-2-yl)-alkanoic acid with oxalyl chloride followed by reaction with a primary amine to obtain 2-(2-alkyl-[1,3]dioxolan-2-yl)-*N*-R^4-alkanamide.

24. The method as recited in claim 23, further comprising: hydrolysis of 2-(2-alkyl-[1,3]dioxolan-2-yl)-alkanoic acid alkyl ester.

25. The method as recited in claim 24, further comprising: reacting of 2-alkyl-3-oxo-alkylic acid alkyl ester with ethylene glycol and *p*-toluenesulfonic acid monohydrate to obtain 2-(2-alkyl-[1,3]dioxolan-2-yl)-alkanoic acid alkyl ester.

26. The method as recited in claim 18, wherein the appropriate carbamide is an appropriate 3-R^3-carbamoylamino-2-alkyl-but-3-enoic acid methyl ester.

27. The method as recited in claim 26, wherein the 3-R^3-carbamoylamino-2-alkyl-but-3-enoic acid methyl ester is cyclized by reacting it with a primary amine and the Grignard reagent.

28. The method as recited in claim 26, wherein the 3-R^3-carbamoylamino-2-alkyl-but-3-enoic acid methyl ester is obtained by acylation of an appropriate 3-amino-2-alkyl-but-3-enoic acid methyl ester.

29. The method as recited in claim 28, wherein the appropriate 3-amino-2-alkyl-but-3-enoic acid methyl ester is obtained by reacting 2-alkyl-3-oxo-butyric acid methyl ester with liquid ammonia.

30. The method as recited in claim 18, wherein the appropriate carbamide is 2-alkyl-3-(2-alkoxy-benzoylamino)-but-3-enoic acid methyl ester.

31. The method as recited in claim 30, wherein the 2-alkyl-3-(2-alkoxy-benzoylamino)-but-3-enoic acid methyl ester is cyclized by reacting 2-alkyl-3-(2-alkoxy-benzoylamino)-but-3-enoic acid methyl ester with phenylmagnesium bromide and primary amine.

32. The method as recited in claim 30, wherein cyclizing the 2-alkyl-3-(2-alkoxy-benzoylamino)-but-3-enoic acid methyl ester yields 2-(2-alkoxy-phenyl)-3-R^4-5,6-dialkyl-3*H*-pyrimidin-4-ones, and

wherein the method further comprises reacting 2-(2-alkoxy-phenyl)-3-R^4-5,6-dialkyl-3*H*-pyrimidin-4-ones with sodium cyanide under microwave irradiation to yield 3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one.

33. The method as recited in claim 30, wherein the 2-alkyl-3-(2-alkoxy-benzoylamino)-but-3-enoic acid methyl ester is obtained by reacting 2-alkyl-3-oxo-butyric acid alkyl ester with liquid ammonia.

34. The method as recited in claim 18, wherein the 2,3,5,6-Substituted 3*H*-Pyrimidin-4-ones is at least one of:

2-(2-hydroxy-phenyl)-5,6-dimethyl-3-phenethyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(2-hydroxy-phenyl)-6-methyl-3-phenethyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-5-propyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-methoxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-5-methyl-3-phenethyl-6-trifluoromethyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-3-phenethyl-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one;

5-cyclopropyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-3-phenethyl-3,5,6,7-tetrahydro-cyclopentapyrimidin-4-one; and

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-3,5,6,7-tetrahydro-cyclopentapyrimidin-4-one.

35. The method as recited in claim 18, wherein R^1 and R^2 are each lower alkyl.

36. The method as recited in claim 35, wherein said lower alkyl is one of methyl, ethyl, propyl, cyclopropyl and isopropyl.

37. The method as recited in claim 35, wherein R^2 is methyl.

38. The method as recited in claim 18, wherein R^1 and R^2 together are $-(CH_2)_n-$ and wherein n is 4 or 3.

39. The method as recited in claim 18, wherein R^1 and R^2 together are at least one of $-(CH_2)_4-$ and $-(CH_2)_3-$.

40. The method as recited in claim 18, wherein R^3 is phenyl optionally substituted with hydroxy.

41. The method as recited in claim 18, wherein
R^4 further comprises the group $-(CH_2)_n-R^5$;
wherein n is 1 or 2; and
R^5 is phenyl optionally substituted with 1 or 2 halogens.

42. The method as recited in claim 41, wherein n is 2 and said halogens are one of fluorine and chlorine.